

The three-noes right-sided infective endocarditis

An unrecognized type of right-sided endocarditis

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Abstract

The “3 noes right-sided infective endocarditis” (3no-RSIE: no left-sided, no drug users, no cardiac devices) was first described more than a decade ago. We describe the largest series to date to characterize its clinical, microbiological, echocardiographic and prognostic profile. Eight tertiary centers with surgical facilities participated in the study. Patients with right-sided endocarditis without left sided involvement, absence of drug use history and no intracardiac electronic devices were retrospectively included in a multipurpose database. A total of 53 variables were analyzed in every patient. We performed a univariate analysis of in-hospital mortality to determine variables associated with worse prognosis. The study was comprised of 100 patients (mean age 54.1 ± 20 years, 65% male) with definite 3no-RSIE were included (selected from a total of 598 patients with RSIE of all the series, which entails a 16.7% of 3no-RSIE). Most of the episodes were community-acquired (72%), congenital cardiopathies were frequent (32% of the group of patients with previous known predisposing heart disease) and fever was the main manifestation at admission (85%). The microbiological profile was led by *Staphylococci* spp (52%). Vegetations were detected in 94% of the patients. Global in-hospital mortality was 19% (5.7% in patients operated and 26% in patients who received only medical treatment, $P < .001$). Non-community acquired infection, diabetes mellitus, right heart failure, septic shock and acute renal failure were more common in patients who died. The clinical profile of 3no-RSIE is closer to other types of RSIE than to LSIE, but mortality is higher than that reported on for other types of RSIE. Surgery may play an important role in improving outcome.

Abbreviations: 3no-RSIE = three-noes right-sided infective endocarditis, LSIE = left-sided infective endocarditis, RSIE = right-sided infective endocarditis.

Keywords: right, sided endocarditis

1. Introduction

Right-sided infective endocarditis (RSIE) is classically considered a benign condition when compared to left-sided infective endocarditis (LSIE). This statement is correct regarding RSIE in intravenous drug users and in patients with cardiac devices. However, a preliminary study showed a mortality rate of 30%, comparable to that of LSIE, in patients with RSIE who are neither drug users nor cardiac device carriers.^[1] This specific type of RSIE has been termed as “the 3 noes right-sided infective endocarditis” (3no-RSIE: no LSIE, no drug users, no cardiac

devices) and represents 16% of all forms of RSIE.^[1] The majority of information on this entity comes from 2 old series.^[2,3] Other groups include LSIE^[4] or, focusing on all types of RSIE, put together a heterogeneous group of patients, some being drug users.^[5] The largest series of exclusively 3no-RSIE is made up of 20 patients.^[1] This study suggests that it seems to be a different entity in terms of clinical profile and prognosis.

Therefore, it is necessary to adequately characterize the clinical, echocardiographic, therapeutic and prognostic profile of 3no-RSIE type in order to make clinicians familiar with this uncommon form of endocarditis. We describe a series of

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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100 consecutive patients with 3no-RSIE compiled from 8 centers with a dedicated team for the management of infective endocarditis.

2. Methods

Standardized protocols, uniform data collection and identical diagnosis criteria throughout the study were used. A total of 53 variables were analyzed in each patient. Only definite episodes of infective endocarditis according to the Duke criteria until 2000 and the modified Duke criteria^[6] afterwards were included. Patients were included in the study if they fulfilled all the following criteria: right-sided endocarditis without left involvement; free of antecedents of drug use; and absence of any type of intracardiac electronic devices. Echocardiographic findings were defined according to the European guidelines on infective endocarditis.^[6] Antibiotic treatment and indications and timing of surgery were decided by the endocarditis team taking into account the recommendations and definitions of the European guidelines. Community-acquired, health-care related and nosocomial endocarditis were defined as considered elsewhere.^[7] The study complies with the ethical principles of the Helsinki Declaration, and was approved by Hospital Universitario de Valladolid ethics committee. The authors from each participating center guarantee the integrity of data.

2.1. Statistical analysis

Categorical variables are reported as absolute values and percentages. Continuous variables are reported as the mean \pm standard deviation or median and interquartile range. Normal distribution of quantitative variables was verified with the Kolmogorov–Smirnov test. Qualitative variables were compared with the chi-squared test and Fisher's exact test. Continuous variables were compared with Student *t* test or its equivalent nonparametric test, Mann–Whitney's *U* test, for variables that were not normally distributed. All data were analyzed with version 20.0 of the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL). Differences were considered statistically significant when $P < .05$.

3. Results

Of a total of 598 consecutive episodes of RSIE hospitalized in the participant centers, 100 were 3no-RSIE (16.7%). These 100 episodes of 3no-RSIE constitute our study group and were retrospectively analyzed.

3.1. Epidemiological characteristics

Mean age at diagnosis was 54.1 ± 20 years and 65% were male. Almost one third (27%) was transferred from other institutions, 72% were community-acquired, 15% health-care related, and 13% nosocomial. Different types of predisposing heart diseases were present in 31% of the patients, being congenital cardiopathies (interatrial septal defects, interventricular septal defects and other complex congenital diseases) the most frequent ($n = 10$, 32%) followed by prosthetic valves ($n = 9$, 29%). The most frequent comorbidities were previous history of cancer ($n = 18$), chronic renal failure ($n = 15$), diabetes ($n = 12$), immunodepression ($n = 11$), chronic obstructive pulmonary disease ($n = 7$), and history of previous episodes of endocarditis ($n = 3$).

A possible focus of the infection was suspected in 59 patients: 20 infected catheters or intravenous lines, 13 skin infections, 4 dental manipulations, 4 gastrointestinal, and 4 urogenital interventions.

3.2. Clinical manifestations

Fever was the main manifestation at the time of presentation (85%), followed by signs and symptoms of heart failure (15%) and cough (10%). Pulmonary embolisms were detected in 27% of the patients. Renal failure at admission was present in 15% and anemia in 33%. During hospitalization, 25% developed heart failure and 10% septic shock.

3.3. Microbiological characteristics

Blood cultures were positive in 90% ($n = 90$) of patients and 10% ($n = 10$) had negative blood cultures. The distribution of the causative microorganisms is depicted in Figure 1. *Staphylococci* were the most frequent microorganisms (36% *Staphylococcus aureus* and 16% coagulase-negative *Staphylococci*).

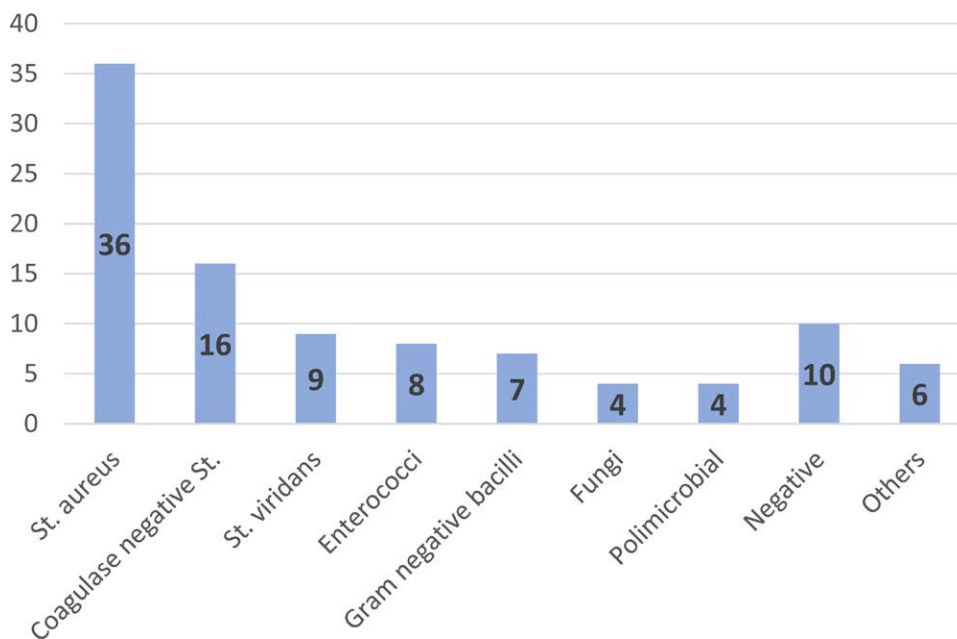


Figure 1. Microbiological etiology distribution of 3no-RSIE. 3no-RSIE = three-noes right-sided infective endocarditis.

3.4. Echocardiographic characteristics

Echocardiographic vegetations were detected in 94% (mean maximum diameter 19.7 ± 9.7 mm), severe valvular regurgitation in 40%, perivalvular complications in 8 (7 abscesses, 1 pseudoaneurysm and 1 fistula; 1 patient had 2 complications). Tricuspid native valve was the most frequent location of the infection (66%), followed by pulmonary native valve (12%), biological tricuspid and pulmonary prosthesis (5% and 4%, respectively), superior vena cava (4%), Eustachian valve (2%), interventricular septum (2%), mural right atrium endocardium (2%), and others (3%).

3.5. Outcome

Hospital stay was 37 ± 20 days. Cardiac surgery was performed in 35% ($n = 35$) patients. Of these, 6 procedures were emergent (17%), 13 urgent (37%), and 16 elective (46%). Indications for surgery were right heart failure ($n = 21$, 60%), uncontrolled infection ($n = 9$, 25%), severe valvular regurgitation ($n = 3$, 9%), and embolism ($n = 2$, 6%). Patients who received only medical treatment ($n = 65$, 65%) had higher mortality than the patients who underwent surgery ($n = 35$, 35%) (26% vs 5.7%, $P < .001$).

In-hospital mortality of the global cohort was 19% ($n = 19$), being multiorgan failure the most frequent cause of death ($n = 8$, 42%). Mortality depending on the therapeutic strategy is shown in Table 1.

3.6. Predictors of mortality

To determine which factors are associated with in-hospital mortality in patients with 3no-RSIE a univariate analysis was undertaken comparing the main characteristics among deceased ($n = 19$, 19%) and recovered ($n = 81$, 81%) patients (Table 2): significant epidemiological variables included non-community acquired infection and diabetes mellitus; significant variables present during the clinical course were right heart failure, septic

Table 1

In hospital mortality depending on the therapeutic strategy.

Therapeutic strategy	Number of patients	In hospital mortality
Emergent surgery	6	0
Urgent surgery	13	1 (7.7%)
Elective surgery	16	1 (6.2%)
Isolated antibiotics	65	17 (26%)

Table 2

Univariate analysis of in-hospital mortality.

	Death ($n = 19$)	Alive ($n = 81$)	P
Age	54 ± 16	54 ± 20	.971
Female	8 (42%)	27 (33%)	.471
Non-community acquired	11 (58%)	23 (28%)	.015
Congenital heart disease	1 (5%)	20 (25%)	.068
Diabetes mellitus	5 (26%)	7 (9%)	.048
Heart failure	9 (47%)	13 (16%)	.011
Renal failure	8 (44%)	5 (6%)	<.001
Septic shock	8 (42%)	3 (4%)	<.001
<i>Staphylococcus aureus</i>	7 (37%)	29 (36%)	.975
Coagulase-negative Staphylococci	2 (11%)	14 (17%)	.854
Enterococci	2 (11%)	6 (7%)	.781
Vegetations	18 (95%)	76 (94%)	.999
Periannular complications	0 (0%)	8 (10%)	.344
Cardiac surgery	2 (11%)	33 (41%)	.013

shock and acute renal failure. Neither microbiological nor echocardiographic variables were associated with higher mortality. Cardiac surgery was associated with higher survival (11% vs 41%, $P = .013$).

4. Discussion

In this work we present the largest series of a poorly studied entity termed as “the 3 noes endocarditis” because it is not left-sided, patients are not drug users and it does not settle on cardiac devices. Remarkable findings about the profile of this very specific type of endocarditis include: it has a quite particular clinical profile, closer to other types of RSIE than to LSIE; however, mortality is higher than that reported on for other types of RSIE; surgery plays an important role in improving outcome; and clinical complications during hospitalization worsen prognosis.

The clinical and microbiological profile of 3no-RSIE resembles the one of RSIE in drug users^[8] but heart failure is as frequent as it is in LSIE.^[9] The microbiological profile may be related to the trigger of infection (central catheters) and to the fact that an increase in *S. aureus* LSIE on native valves has been shown in recent years.^[10] Thus, despite resembling the clinical profile of RSIE in drug users, mortality is closer to that reported on for LSIE.^[11] The reason cannot be inferred from our results. We can speculate that physicians taking care of these patients are not fully aware of the poor prognosis of this subset of RSIE and do not consider surgery as a first therapeutic option. Regarding the results of our series, less patients underwent surgery than the reported on for LSIE.^[12] We might speculate that a more active therapeutic approach, as it is taken for LSIE, considering surgery as an option in the early phases of the disease could improve outcome.

Several epidemiological and clinical characteristics were significantly more frequent in patients who died. Diabetes has been shown to increase the probability of several infectious diseases. Diabetic patients bear deficient host immune mechanisms of defense, hyperglycemia negatively affects different properties of leukocytes, including phagocytosis, migration and chemotaxis and microvascular dysfunction may lead to delayed response to infection.

Regarding variables pertinent to the clinical manifestations of the disease, right heart failure, septic shock and acute renal failure were more frequent in patients who died. All have been found to predict outcome in LSIE^[9,13,14] and it is not surprising their impact in our population. Interestingly, our results show that right heart failure in 3no-RSIE, as a manifestation of valve dysfunction secondary to destruction of valve tissue, bears the same prognostic power that left heart failure in LSIE. Given that only surgery can solve that situation, the fact that few patients were sent to surgery reinforce the relationship between heart failure and death. Septic shock and renal failure represent a more advanced state of the disease, which has progressed from a localized state to become systematic. Thus, these manifestations may be less prone to be influenced by surgery.

We are aware of several limitations present in our work. Being the number of patients quite high for an unusual disease, the sample size is not enough to undertake a multivariable analysis to identify predictors of outcome; thus, conclusions cannot be regarded as definitive. Centres participating in the study are reference for infective endocarditis and patients with a more benign clinical course not sent to our centers may have been missed. Finally, given the limitations inherent to the retrospective gathering of data, our results may be biased.

To summarize, RSIE in non-drug users who do not bear cardiac devices (“the 3 noes endocarditis”) has a clinical profile similar to classic RSIE but with a high mortality rate. Surgery should be considered in the therapeutic strategy as soon as a diagnosis is established.

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Writing – review & editing: Gonzalo Cabezon, Javier Lopez.

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